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Effects of low intensity muscle training with vascular occlusion on muscular strength and endurance

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Abstract

This study investigated whether ischemic exercise training (TR_{IS+EX}) would increase endurance of ischemic (EX_{IS}) and ramp (EX_{RA}) knee extension tests more than exercise training (TR_{EX}) alone. Ten healthy subjects participated pre- and post-tests with each leg. For EX_{RA}, after warm-up a weight was added each min until exhaustion. EX_{IS} was similar, but after warm-up, a thigh cuff was inflated to 150 mm Hg instead of adding weights. One leg was chosen for TR_{IS+EX} (cuff inflated to 150 mm Hg during exercise) and the other for TR_{EX}, both with a small weight on each leg, 4-6 times for 3-5 min each per daily session, 5 days per week for 6 weeks. EX_{IS} duration increased 120% more ($P=0.002$) in the TR_{IS+EX} leg than in the contra-lateral TR_{EX} leg, whereas EX_{RA} duration increased only 16% (NS). TR_{IS+EX} and TR_{EX} significantly attenuated the ventilation increase (ergoreflex) during EX_{IS}. The O_2 debt for EX_{IS} was significantly lower and systolic blood pressure recovery was faster after TR_{IS+EX} than after TR_{EX}. Heart rate recovery after EX_{RA} and EX_{IS} was faster after TR_{IS+EX}. Apparently TR_{IS+EX} with low-intensity resistance increases exercise endurance and attenuates the ergoreflex and

therefore, may be a useful tool to increase regional muscle endurance in order to improve systemic exercise capacity in patients.

INTRODUCTION

Exercise intolerance is one of the most prominent features of acute or chronic activity-disabling diseases such as congestive heart failure and chronic obstructive pulmonary disease. Many studies suggest that enhanced exercise capacity is associated with increased quality of life and longer survival[1]. However, these chronic diseases may restrict sufficient exercise intensity that is necessary to provide an adequate training stimulus and these patients often cannot perform sufficient activity to avoid progressive deconditioning.

Any peripheral exercise stimulus that prevents deconditioning or enhances training can be very beneficial for patients with a disable disease. Training groups of skeletal muscles, e.g. leg muscles collectively required for large motor activities (e.g. walking, stair-climbing, cycling), without taxing the central circulation can improve whole body exercise capacity and metabolic performance of patients with congestive heart failure[2, 3] which are the ones most commonly studied. Intense regional training of larger muscle groups does place significant demand on the central circulation, so additional strategies to enhance aerobic capacity and endurance in these muscle groups important to daily life could offer additional help to the patients, especially those having congestive heart failure.

It has been shown that peak exercise performance is enhanced in healthy subjects by reducing blood flow to exercising muscles by 20% during training with lower body positive pressure[4]. It has recently been reported that vascular occlusion during high-intensity resistance exercise training of arm flexors can induce favorable biochemical changes in the muscle[5]. It is not known,

however whether a reduction in blood flow during repeated exercise bouts with low-intensity workloads, appropriate for chronically ill patients, would also enhance muscle training.

The purpose of the present study was to determine whether repetitive, low-intensity dynamic knee extension exercise with marked reduction of blood flow (ischemic training) would increase work capacity of the knee extensors more than the same exercise without ischemia.

METHODS

Subjects. Then, 5 males and 5 females, volunteered as subjects. Informed, written consent was obtained from each. Their mean age and BMI were 50 yr and 23.5 k/gm^2, respectively, ranging from being sedentary to jogging or cycling daily for 30 min. Exclusive criteria included hypertension, any history of venous or arterial thrombosis, lower extremity arthritis, blood clotting abnormalities and evidence of central or peripheral vascular disease.

Muscle exercise test. Maximal ramp and endurance knee extension tests were conducted on an exercise chair. Exercises were done to a metronome, whereby both knees alternately extended completely and relaxed through a 90° range so that each leg performed 20 knee extensions per min. For the ramp test (EX_{RA}), after resting measurements, the subject exercised for 2 min with no load added to the weight of the swing arms. At the mid point of the leg range of motion, the weight of the chair arm was 4.1 kg. Each succeeding minute, a 2.3 kg weight was added to the swing arm on the side of the leg being tested. This was continued until the subject could no longer fully extend that knee or keep up with the metronome rhythm. For the ischemic endurance test (EX_{IS}) the same exercise was performed, but after 2 min of baseline exercise, a cuff (Hokanson Co., Bellevue, WA), previously placed on the upper thigh, was

inflated to 150 mm Hg. This occlusion pressure was maintained until the exercise end-point was reached, based on the same criteria as the ramp test.

Experimental protocol. Subjects were screened, enrolled in the study and familiarized with the testing procedures. Pre-training testing consisted of EX_{RA} performed on the left leg and then the right. Then EX_{IS} testing was done on the left leg, followed by the right, with a 15-min rest between each test., A 6-week training period, with the same leg always made ischemic by an inflated cuff during the exercising training, was followed by repeating the same tests. A comparison of pre- and post-training measurements of each leg's exercise test duration and associated variables during EX_{RA} and EX_{IS} was used to evaluate changes attributable to ischemia during training.

Training protocol. During training the subjects performed the same exercise as for EX_{IS}, with a 1.1 kg weight (approximately 3% of maximal voluntary contraction, MVC: range 2-4%) attached to each ankle, on a chair or bench in the laboratory or at home. Subjects performed knee extensor exercise with each leg 4 to 6 times per daily session for 3 to 5 min each, 5 days per week for 6 weeks. In these training exercises the blood flow in the ischemically trained leg was reduced with a thigh cuff inflated to 150 mm Hg (TR_{IS+EX}) and the other leg was exercised without the cuff (TR_{EX}). The 4-6 bouts of 3-5 min each were chosen as the exercise goal to achieve a total training time of 20 min. Preliminary trails indicated that 3-5 min of ischemic exercise could be tolerated. As training progressed, if the subjects were able to increase bout duration, the number of bouts decreased to maintain the 20 min of exercise training each day.

Metabolic measurements. Gas exchange was measured before, during and for 3 min after the exercise testing utilizing a TrueMax 2400 breath-by-breath automated system (Parvomedics Inc., Sandy, UT) with incorporated software. These measurements included oxygen uptake (VO_2), carbon dioxide out put

(VCO_2) and pulmonary ventilation (V_E). The O_2 debt was estimated from the VO_2 during the 3 min recovery, minus pre-exercise resting VO_2. A single-lead ECG was used to obtain heart rate (HR). The systolic blood pressure (SBP) was measured by an arm sphygmomanometer at baseline rest and for each min during and after exercise the same investigator.

EMG recording. Surface electromyograph (EMG) recordings during EX_{RA} and EX_{IS} were made to estimate differences in muscle fiber recruitment and fatigue during exercise. In addition to the inability to complete knee extensions, a shift to lower frequencies of motor unit firing rates in the power spectrum of the quadriceps EMG was used to confirm a similar degree of muscle fatigue[6]. The EMG analyses from a single channel recording from the vastus lateralis were performed with a Naroxon 1200system (Soottsdale, AZ). Skin preparation for electrodes included shaving, sanding and cleaning the skin with alcohol on the patella and on the vastus lateralis 2 and 4 cm proximal to the patella. The reference electrode was placed on the patella and the two recording electrodes were placed on the vastus lateralis and remained there for the entire session for the ramp and ischemic test. Both raw and rectified EMGs were collected for the last 5 bursts (contractions) of each minute of each exercise. By computer processing, these bursts were averaged and analyses were performed, including integrated EMG (iEMG) and spectral analysis by fast Fourier transform. Total spectral power and mean and median frequencies were analyzed. The shift in frequency of the entire power spectrum with exercise duration was calculated from the area of the cumulative distribution function of the frequency spectra and expressed as percent change from baseline exercise.

Data analysis. Each subject's leg trained by TR_{EX} without ischemia served as a control comparison for the leg trained by TR_{IS+EX}. The differences between the post-pre-training changes in exercise duration in each leg were compared by paired t-test.

Similarly, the differences in changes in EMG paprameters and gas exchange measurements between the pre-training and post-training tests were taken to represent the differences resulting from ischemic training. Differences in recovery values were tested by 2-way (time and group) ANOVA, with values at specific times compared by Tukey's *post hoc* test.

RESULTS

Exercise duration. The average durations for exercise tests before and after training are shown in Fig. 1 and Fig. 2. In Figure 1, the duration of EX_{IS} increased 0.8min (16%, NS) after TR_{EX} and 5.5 min after TR_{IS+EX}, a difference of 120% (P=0.002).

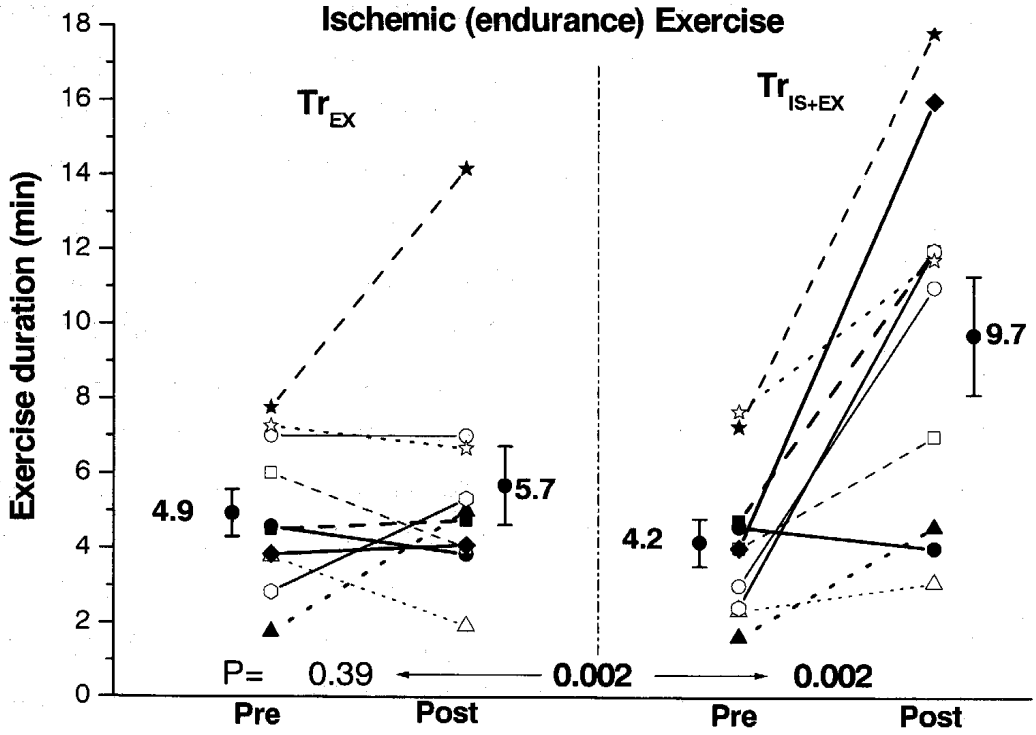

Figure 1. Changes in exercise duration in 10 subjects for ischemic endurance test before and after training. TR_{IS+EX}: leg trained by ischemia + exercise; TREX: leg trained by exercise only. The average times are indicated in Table 1. The difference between the change in ischemic exercise duration after TRIS+EX and after TREX is significant (P=0.002).

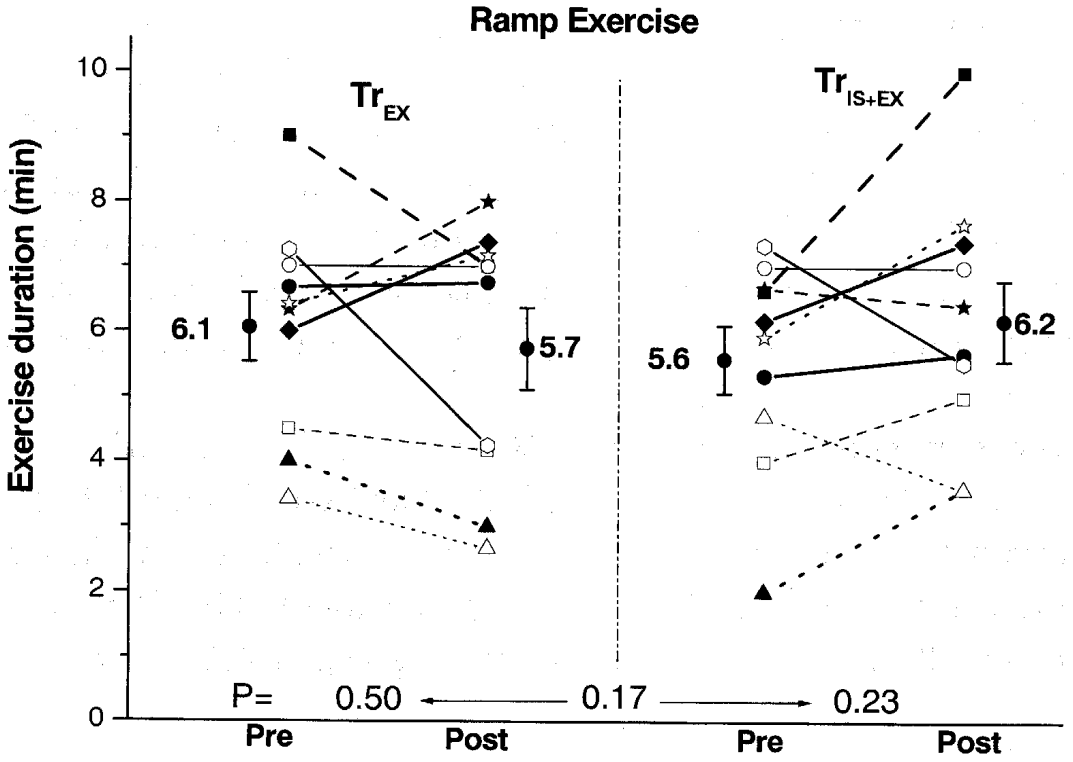

Figure 2. Changes in exercise duration in 10 subjects for ramp test before and after training. TR_{IS+EX}: leg trained by ischemic + exercise; TR_{EX}: leg trained by exercise only. The average times are indicated in Table 1.

For EX_{RA}, the maximal workload is proportional to the test duration; the leg trained by TR_{EX} had a small reduction in EX_{RA} time from 6.1 to 5.7 min and for the leg trained by TR_{IS+EX} the duration increased from 5.6 to 6.2 min (Fig. 2). This 21% difference, corresponding to ischemic training, was positive in 7 to 10 subjects, but not statistically significant ($P=0.17$). The Cohen's-d and effect size values for the differences in exercise duration with training were 1.39 and 0.57 for EX_{IS} and 0.63 and 0.30 for EX_{RA}, respectively.

To determine whether pre-training fitness level for this exercise influenced the results, we divided the 10 subjects into two groups of 5 each, based on a ranking of their average time on the pre-tests for both legs on the ischemic and ramp knee extension tests. The average time for the highest ranked group ("trained" −6.3 min) was significantly ($P=0.007$) above that of

the other ("untrained" −4.1 min). Both groups increased their time on the ramp exercise by 0.9 min and the ischemic exercise by 4.8 min. The percent increases were 13% for trained and 30% for untrained (P=0.55) on the ramp test and 108% for "trained" and 141 % for "untrained" (P=0.65) on the ischemic test. Therefore, the pre-training exercise capacity did not have a significant influence on the improvement with raining for this type of exercise.

Oxygen consumption. The VO_2p ranged from 685 to 789 ml/min in the four EX_{IS} tests (2.4-2.8 Met) and from 949 to 1062 ml/min (3.4-3.8 Met) in the four EX_{RA} tests. The cumulative 2 uptake above resting levels is shown in Table 1. The O2 used for the first 2 min of warm-up exercise averaged 479 ml for all 8

Table 1.

Ischemic and ramp exercise duration and O_2 consumption of 10 subjects

			duration	cumulative O_2 consumption		
			cuff or ramp (min)	cuff or ramp (ml)	recovery (ml)	recovery/total (%)
Ischemic exer.	Tr_{IS+EX}	Pre	4.2	1784	376	17.4
		Post	9.7	3375	308	8.4
		Post-Pre	**5.5#**	**1591#**	-68	-9.0
	Tr_{EX}	Pre	4.9	2018	274	12.0
		Post	5.7	1909	328	14.7
		Post-Pre	0.8	-109	54	2.7
	Tr_{IS+EX}-Tr_{EX}	Post-Pre diff	**4.7&**	**1700&**	**-122&**	**-11.7&**
Ramp exer.	Tr_{IS+EX}	Pre	5.6	3134	861	21.6
		Post	6.2	3456	662	16.1
		Post-Pre	0.6	322	**-199#**	**-5.4#**
	Tr_{EX}	Pre	6.1	3388	649	16.1
		Post	5.7	2819	529	15.8
		Post-Pre	-0.4	-569	-120	-0.3
	Tr_{IS+EX}-Tr_{EX}	Post-Pre diff	1.0	891	-79	**-5.1&**

Tr_{IS+EX}: leg trained with exercise plus ischemia; Tr_{EX}: leg trained with exercise only
#: value sign. different ($p<0.05$) between pre- and post-training
&: difference value sign. different between exer+isch and exer training
cuff or ramp: oxygen used for total exercise after baseline (warm-up) exercise
recovery: oxygen consumption above resting level during 3 min after exercise

tests. The O2 cost during exercise after the warm-up corresponded with duration, as expected. After EX_{IS} the recovery O_2 was significantly reduced after TR_{IS+EX} compared with TR_{EX}. After training, the recovery O_2 decreased for both legs in EX_{RA}, but was only significant in the TR_{IS+EX} group. The recovery O_2 as a percentage of the total O_2 cost was also reduced significantly more by TR_{IS+EX} than TR_{EX} and this difference was significant after both EX_{IS} and EX_{RA}.

Pulmonary ventilation. The V_E changes for EX_{IS} are shown in Figure 3. After ischemic training, the maximal V_E was significantly lower than the pre-training maximal value, even though the exercise duration was more than doubled (Fig. 3-A). The V_E attenuation was even greater comparing the pre-training V_E at maximal exercise to the post-training V_E at the same exer-

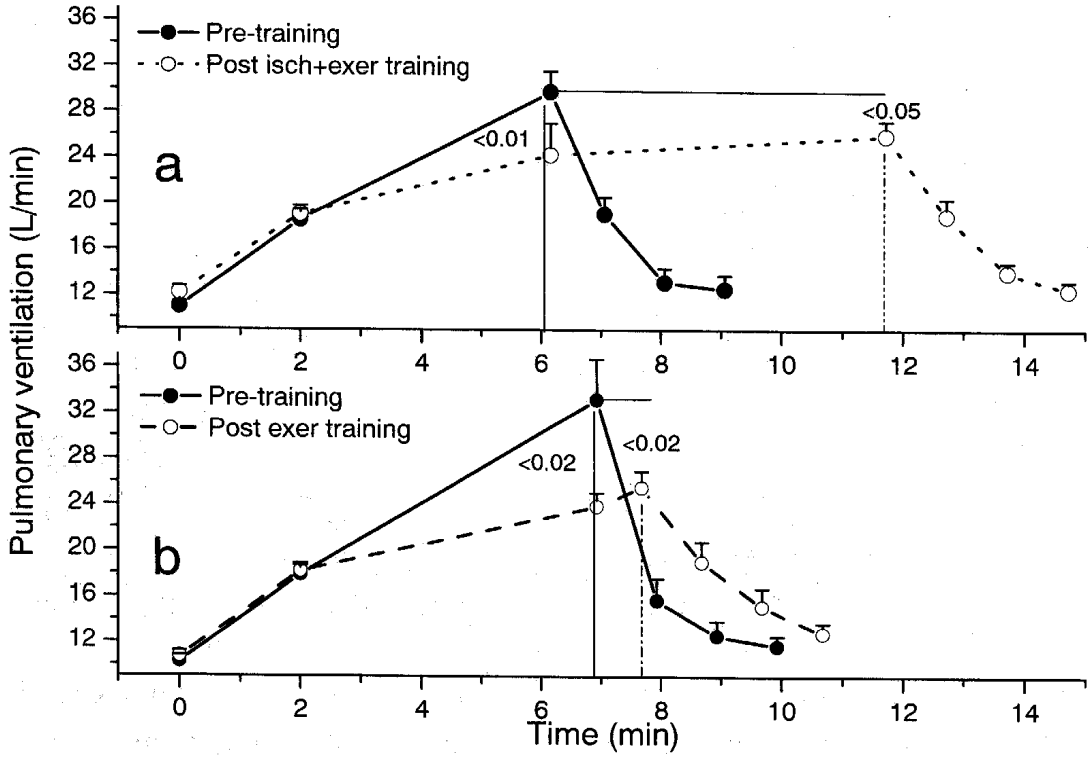

Figure 3. Mean (±SE) of V_E for 10 subjects during rest, warm-up (baseline) exercise for 2 min, ischemia + exercise training. Significance of the difference from the pre-training maximal values are indicated.

cise time. For the TR_{EX} leg, there was also a significant reduction in V_E after training, even though this exercise duration was not significantly increased (Fig. 3-B). During EX_{RA} the V_E increased similarly for all four tests from warm-up to VO_2p, by an average of 18L/min (98%).

Heart rate and SBP recovery after exercise. After TR_{IS+EX} there was a faster recovery for HR and SBP following EX_{IS}. After EX_{RA} the HR (Fig. 4) and SBP (Fig. 5) also both recovered faster after TR_{IS+EX}, but only the former was significant. The rate-pressure-product in the four ischemic exercise tests at maximal exercise averaged 15,800 (SE: 990).

EMG recording. Typical frequency spectra and calculations are shown in Fig. 6 for one subject. The frequency power spectra were always skewed to the right, with peak power (mean fre-

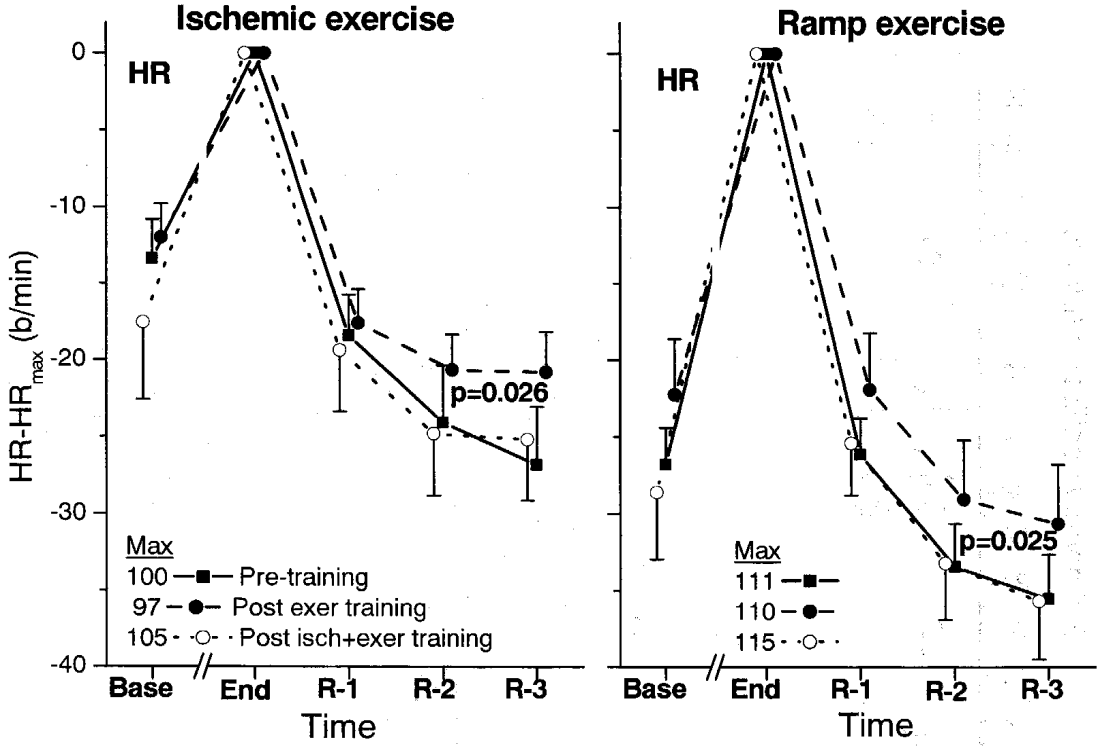

Figure 4. Mean values for 10 subjects for ischemic and ramp exercise for HR during baseline and maximal exercise and during 3 min of recovery, before and after training with exercise and ischemia + exercise. All values are shown as a difference from the maximal exercise value, with the two pre-training tests averaged.

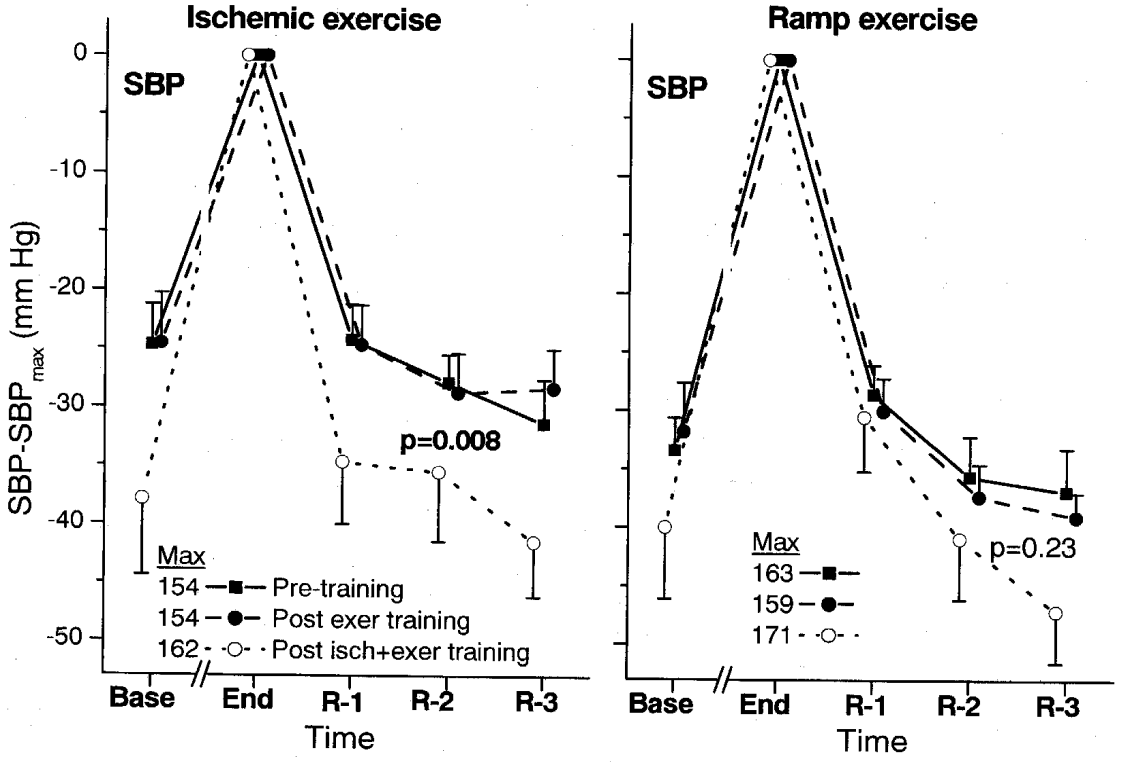

Figure 5. Mean values for 10 subjects for ischemic and ramp exercise for SBP during baseline and maximal exercise and during 3 min of recovery, before and after training with exercise and ischemia + exercise. All values are shown as a difference from the maximal exercise value, with the two pre-training tests averaged.

quency) occurring at an average of 62.4 (SE: 1.0) H_Z during the baseline warm-up exercise before ischemia or workload increments were imposed. The shift to lower motor unit firing frequencies during the course of the exercises was taken as an estimate of motor unit fatigue and changes in the power (area under the curve) were considered proportional to recruitment of motor units. The average frequency shifts from baseline to peak exercise values were not significantly different between EX_{IS} and EX_{RA} or between recordings before and after training. During EX_{RA} there was the same reduction in frequency of 14% from baseline to maximal workload for tests before and after TR_{EX}. In the TR_{IS+EX} leg, the shifts were −8 and −9% before and after training, respectively. For EX_{IS} the frequency shift was −6before TR_{EX} and −11% after TR_{EX} ($P=0.12$), but −6 and −4%

before and after training in the TR_{IS+EX} leg ($P=0.27$). These differences in frequency shifts were not statistically significant ($P=0.11$). The total power during EX_{RA} (Fig. 6) increased from baseline to maximal exercise by an average of 720%, indicating increased recruitment, and by a factor of 40% for EX_{IS}, with no significant changes or differences in changes related to training.

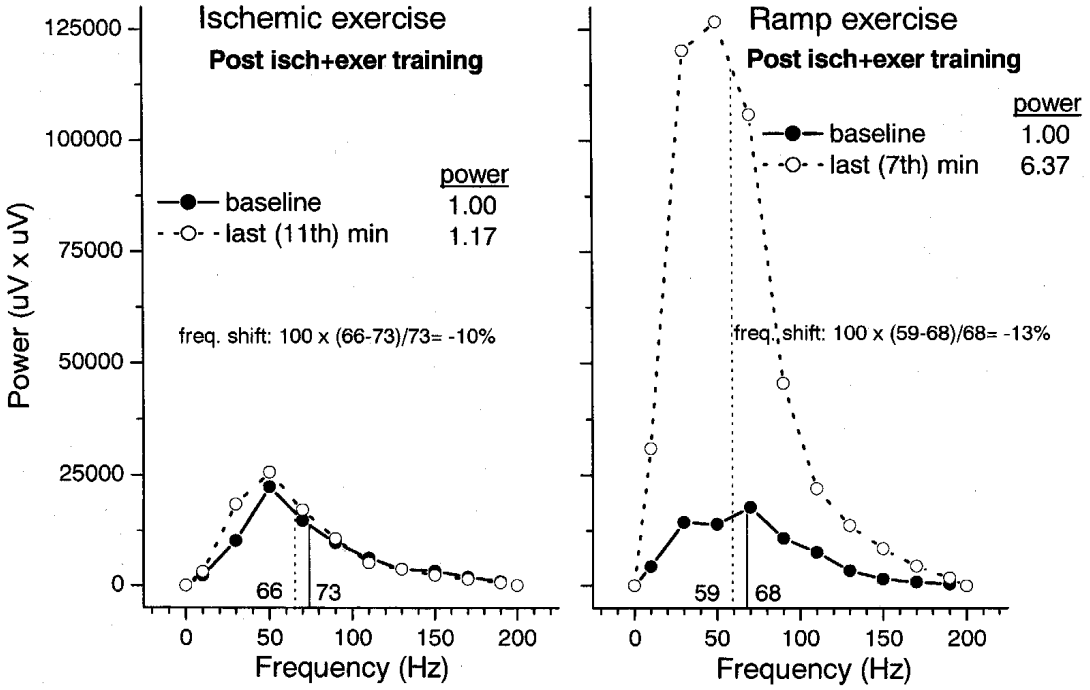

Figure 6. Typical recordings from one subject, of frequency spectra as processed by fast Fourier transform, averaged from 5 contractions in a subject after ischemia + exercise training during the last 15 s of baseline exercise and during the last minute of ischemic and ramp exercise tests. Power increased by a factor of 6 during ramp exercise, indicating increased fiber recruitment with increasing load, but remained about the same for ischemic exercise. The mean frequency shifted to a lower value from start to end of exercise, indicating increasing fatigue, i.e., 100 X (66-73)/73 = −10% for EX_{IS} and 100 X (59-86)/68 = −13 for EX_{RA}.

DISCUSSION

The result of this study demonstrated that training with a combination of ischemia and low-resistance exercise increased knee extension exercise endurance under ischemic conditions. The effect of TR_{IS+EX} on exercise with no ischemia could not be measured because he workload was too light for end-points to be obtained. Earlier studies have noted significantly greater improvement in time-to-fatigue and one-legged VO2p in ergometer exercise in legs trained for 45 min/day for 4 days/week for 4 weeks with a 20% blood flow reduction, as compared to control legs training without flow restriction[6]. Similar to our results, those improvements in the ischemically trained leg were greater when the test was performed with flow restriction than without flow restriction, demonstrating specificity in the training response. Other measurements during those studies, including muscle biopsies, determined that ischemic training contributed to higher citrate synthase activity, lower lactate dehydrogenase isoenzymes, more type- I and few type- II fibers and more capillaries/fiber[7]. More recently, it has also been demonstrated that ischemically trained legs increased in cross-sectional area, probably resulting from increases in contractile proteins, intracellular water and mitochondrial volume[8, 9]. Minimal hypertrophy in either leg after endurance training, with or without ischemia, at these low levels of MVC (4%) and non was noted. However, increased capillarization and improved O2 delivery would be expected. Studies in rats have shown that restricting blood flow during high resistance training of an exercising limb enhanced exercise capacity corresponding to an increased arteriolar capillary density[10]. All of these studies demonstrated that training using usual training intensities under ischemic conditions enhanced aerobic exercise capacity.

The main difference between those studies and the current

one is that this study used much controls. In this study there was no significant training effect on exercise duration from training without ischemia, implying that this level of exercise intensity will not induce training by itself. And yet, using the same training intensity under ischemic conditions provoked a marked increase in exercise endurance, confirming the unique contribution of ischemia to exercise training. The starting fitness level to knee extensions did not significantly alter the improvement from the training.

In the benefits of exercise training most important, particularly to heat failure patients, is the improvement in exercise dyspnea and heart rate. The effect of training on these endpoints can be measured by the "ergoreflex" or muscle chemoreflex response to ischemia imposed during exercise. The usual physiological "rgreflex" parameters measured include ventilation, blood pressure and heart rate during and after ischemic exercise.

The attenuation of V_E during EX_{IS} after TR_{IS+EX} and TR_{EX}, shown in Figure 2 is striking. An equivalent reduction in V_E during EX_{IS} in response to ischemia in the leg not training by ischemia (TR_{EX}) suggests that the central site of the afferent limb of the ergoreflex was affected by the training, not only the site of origin in the exercising muscle.

The main ventilatory stimulus from regional ischemia is thought to be the local concentration of H^+ [11]. Eiken and Bjurstedt[12] demonstrated that venous lactate concentration, V_E, arterial blood pressure, HR and V_E/CO_2 were significantly greater and VO_2p was reduced by leg ischemia compared with no flow restriction. In the present study, he reduced O_2 uptake in recovery from EX_{IS} after TR_{IS+EX} (Table 1) suggests that ischemic training between the O_2 debt, presumably by reducing accumulation of lactate and H^+ during exercise and therefore the release of these metabolites was diminished when exercise terminated and cuff pressure was released. This trend was has

pronounced after EX_{RA}, where the O_2 debts were larger and the decline in the percent of the total cost was smaller, but still significant.

The recovery patterns of HR and SBP in Figs. 4 and 5) indicate that TR_{IS+EX} contributed to a faster recovery for both circulatory variables after EX_{IS}, with some carryover benefit indicated for HR after EX_{RA} ($P=0.008$). More rapid recovery rates of SBP[13] and HR[14] following exercise, associated with vagal activation and sympathetic deactivation, are known to be directly related to exercise capacity and inversely to mortality in patients with heart failure.

These findings suggest that blood flow restriction to the legs during exercise places additional metabolic stress on exercising muscles, enhancing the sympathetic response to exercise at a given workload compared with no ischemia. If metabolic stress to the muscles is the stimulus for a training response, then flow restriction should augment the leg training response. Ergoreflex responses are enhanced in patients with congestive heart failure, presumably because of peripheral muscle effects of the disease[15, 16] and are reduced by non-ischemic endurance training in these patients[7].

EMG recordings made during progressive exercise demonstrate a shift to lower EMG frequencies, presumably because of a large contribution of slow twitch muscle fibers (type I, having slower firing rates) as fast twitch (type II) fibers fatigue[18, 19]. This shift might also occur partly because of a decrease in average nerve conduction velocity of motor units. Type II motor units operate with a faster nerve conduction velocity than do type I fibers and as they fatigue first the average nerve conduction velocity decreases as they are recruited less[20]. In the present study, the difference in frequency shift between control (TR_{EX}) and TR_{IS+EX} legs was not significantly different for either test exercise. This means that the rate of the shift with exercise time was decreased during EX_{IS} because duration was

more than doubled. However, with the low exercise intensity (<4% MVC) utilized in the ischemic training, it is doubtful that type II fibers were significantly utilized or trained in these exercise [21] and the local ischemia probably affected them minimally. A previous study has found that ischemia induced during an endurance exercise did not result in a frequency shift[19]. This suggests that the slower frequency shift with time of exercise after ischemic training may have resulted from an endurance training effect on type I fibers. These findings are in line with those of Esbjornsson et al.[7], who reported more aerobic or endurance type- I and fewer type-IIB fibers with ischemic training.

Other strategies to improve muscle O_2 delivery during training have been tested. Intermittent systemic hypoxic training has been used in healthy subjects to improve athletic performance[22] and improve muscle energy supply during normoxic exercise[23]. For peripheral skeletal muscles, ischemic training may be more effective than hypoxic training because with ischemia the venous effluent blood has much higher PCO_2 and H^+ concentrations, reflecting changes in the perfused tissue s[24], than with hypoxia causing the same reduction in O_2 delivery. In addition to providing a stronger training stimulus, regional ischemic training is safer to apply than systemic hypoxemia. For a given rduction in mixed venous O_2 level, the arterial oxygenation remains higher so that O_2 delivery to critical organs (e.g., brain, heart, and kidney) is not restricted and studies utilizing complete occlusion of limbs during exercise in congestive heart failure patients have been done without any reported risk.

This study shows that endurance training can be achieved with dynamic, low intensity resistance exercise with superimposed ischemia. Other studies have shown that ischemic training increase exercise tolerance in healthy individuals during high resistance exercise[5, 6, 8] and general endurance training at-

tenuates the ergoreflex and resulting dyspnea in patients with congestive heart failure[17, 25]. Therefore, it seems probable that ischemic training would further reduce dyspnea, sympathetic responses and improve skeletal muscle metabolism and exercise capacity especially in patients with congestive heart failure or other chronic diseases. Exercise training can improve exercise performance, quality of life and improve endothelial function in non-exercising vascular beds in patients with chronic heart failure[26]. Ischemic training might also broaden the population of patients who could be trained since regional ischemic training could be implemented in patients not typically able to comply with rehabilitation programs requiring more intense systemic training. Further studies will help define the role that ischemic training will have in enhancing he daily lives of patients with chronic disease characterized by inactivity.

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